women aged 30 to 40 and from 60 to 70. I understand that the results accord closely with a survey carried out by Dr. F. I. Caird and Dr. G. A. Middleton in Oxford. From Table I it will be seen that in the first decade men accounted for 49.4% of the under 50s and 25.9% of those aged 50 and over. In the second decade the respective figures were 43.2% and 38.2%.

INFLUENCE OF HOSPITALS

Use of the hospital services in the Hartlepool has increased from 21,672 (deaths and discharges plus new outpatients) in 1949 to 29,241 in 1968. Mild cases of diabetes may have been found from inpatient and outpatient departments. Mild diabetes in patients aged 50 and over is sometimes difficult to diagnose on clinical grounds alone. Acute symptoms are often missing, unless there is infection or injury, and slight thirst, loss of weight, and lethargy may go unnoticed. Of those aged 50 or over in this series 17.7% of men and 26.0% of women waited for six months or more before seeking advice. Pruritus vulvae was noted as a symptom in 89.4% of females. Balanitis in males is uncommon, and only 4.1% were affected by it. Other diagnostic factors were a family history of diabetes in 26.2% of females and 32.4% of males, while 41% of females and 18.6% of males had children whose birth weight was 8 lb (3.6 kg) or more at birth, and 66.1% of females and 36.6% of males were themselves overweight.

To test the influence of the hospital services on diagnosis the source of diagnosis in the series were examined. In the first decade 30% of the males and 19.1% of the females aged 50 and over were first diagnosed in hospital as against general practice. In the second decade the comparable figures rose respectively to 38.1% and 31.6%. Among the reasons for hospital reference were the following: respiratory disease 9, cardiovascular disease 18, cerebrovascular disease 6, injury 8, infections and ulcers 18, balanitis 6, non-acute operations 4, acute operations 4, pruritus vulvae 15, cataract 16, retinitis 15, and visual defects 15. The figures are for the number of cases in each category. Two cases were referred with diarrhoea and three with upper abdominal pain due to ketotic precum. But most of the cases were picked up as a result of routine urine examinations.

DISCUSSION

The pronounced change in the proportion of men aged 50 and over in the second decade, from 25.9% to 38.2%, needs further consideration. It is stated that in the last century male diabetics predominated, but that a change started at the end of the century. During the first half of this century females predominated in most clinics in Britain. However, recent surveys suggest that the ratio is changing again (Malins, Fitzgerald, and Wall, 1965), but it is uncertain whether the change is due to an increase in men or a decrease in females. With the Hartlepool figures the drop in the female rate might be accounted for by a stabilization of the clinic intake. But the rise in the male rate in the second decade is too pronounced and too quick to be accounted for by a general rise in the male diabetic population in this age group.

That 38.1% of men aged 50 and over were diagnosed in hospital suggests that routine urine examinations are important in finding mild cases of diabetes without obvious clinical symptoms. Some might have been diagnosed earlier and some were probably missed, since urine examinations are not always done after a recent, reasonably high carbohydrate meal. While the proportion of males diagnosed in general practice fell slightly in the second decade as compared with those diagnosed in hospital, the actual number of cases in patients aged 50 and over and diagnosed in general practice rose from 42 to 102. The whole picture suggests a greater awareness of the possibility of diabetes as a diagnosis, and the presence of an active local diabetic clinic may have played some part in this.

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REFERENCE


MEDICAL MEMORANDA

Disseminated Intravascular Coagulation Complicating Infectious Mononucleosis

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Disseminated intravascular coagulation is a rare complication of viral infections. In the case reported here it was associated with infectious mononucleosis.

Case Report

A 15-year-old girl was admitted to hospital with a history of onset of sore throat and cervical lymphadenopathy 14 days previously followed by fever, rigors, malaise, and vomiting which were not relieved by tetracycline. On admission she was dehydrated. She was not jaundiced and had no purpura or bruises, but there were tender, enlarged lymph nodes in the neck and axillae and the tip of the spleen was palpable. The red cells were normochromic and normocytic, and neither then nor later were there any fragmented cells. Most of the leucocytes were abnormal mononuclear cells which were interpreted as glandular fever cells. The haemoglobin was 10.2 g/100 ml and a blood count showed R.B.C. 4,000,000/mm³, platelets 15,000/mm³, W.B.C. 2,900/mm³ (granulocytes 2%, monocytes 2%, metamyelocytes 27%, glandular fever cells 69%). Liver function tests: SGOT 186 units/ml, SGPT 80 units/ml, albumin 2.9 g/100 ml, globulins 19/100 ml, and bilirubin 0.3 mg/100 ml. A marrow aspirate yielded only blood.

The patient was given intravenous fluids and, after blood had been taken for culture, cephaloridine 1 g four times a day. After two days the fever had not remitted. Blood cultures were negative, and in an effort to make a diagnosis a further bone marrow aspirate together with a bone trephine was taken from the iliac crest. The aspirate again yielded only blood but the trephine was cellular and contained...
many large cells of histiocytic type with central nuclei and clear cytoplasm. The cells were interspersed with numerous smaller mononuclear cells. Several hours after the trephine was taken it became apparent that the patient had developed a bleeding tendency which was more severe than could be accounted for by the thrombocytopenia. There was haemorrhage from the trephine site and large bruises developed around the sites of earlier venepunctures (see Fig.).

Coagulation studies demonstrated only hypofibrinogenaemia. The fibrinogen level was 25 mg/100 ml (normal 200 to 400 mg/100 ml) and the fibrinogen titre was 1/16 in aminocaproic acid (EACA) and in saline (normal 1/256). No significant fibrinolysis could be detected. The euglobin clot lysis time was normal and fibrin degradation products were at the upper limit of normal at 4 μg/ml (Merskey et al., 1969). It was decided that the patient had disseminated intravascular coagulation. She was given two units of fresh blood and a continuous intravenous infusion of heparin, 12,000 units in 24 hours, for seven days. Within 24 hours her plasma fibrinogen level had risen to 92 mg/100 ml, she was afebrile, and was feeling well. Seven days later the fibrinogen level was 300 mg/100 ml.

The Paul-Bunnell test was negative on three occasions during the patient’s four weeks in hospital and again one month after her discharge. The Epstein-Barr virus antibody titre rose from 1/128 while in hospital to 1/2,048 six months later. It was not measured in between. There was no rise in antibody titre to cytomegalovirus. On discharge the blood picture was virtually normal with only 2% of atypical mononuclear cells. Recovery was complicated by loss of power and sensation in the left hand owing to compression of the radial and median nerves at the elbow from haemorrhage round the joint.

Comment

The highly significant rise in EB virus antibody titre associated with the typical blood picture are enough proof that the defibrination was associated with infectious mononucleosis. The cause of the defibrination and pancytopenia is not clear. It was most probably due to low grade, diffuse intravascular coagulation, which would account for the thrombocytopenia and the low fibrinogen level. This must have begun before admission to hospital but manifested itself on the day the trephine was taken. Alternatively, bearing in mind the abnormal liver function tests, it could be speculated that the hypofibrinogenaemia was a production defect. However, this is unlikely in view of the rapid response to heparin. The granulocytopeny and in part the thrombocytopenia might have been an expression of the effect of the virus on the bone marrow.

McKay and Margaretten (1967) reviewed case reports of the association between viral infections and fibrinogenemia. The arboviruses—for example, those causing the various haemorrhagic fevers which occur in the tropics, and the exanthematous viruses (varicella, variola, rubella)—are those which are most commonly implicated. Glandular fever was not included in their list, but Wintrobe (1967) mentions one patient who developed hypofibrinogenaemia during the course of the disease. All authors agree that the treatment of choice is intravenous heparin.

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References


Complication of Methotrexate-maintained Remission in Lymphoblastic Leukaemia

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As more patients with acute lymphoblastic leukaemia are being maintained in remission for longer periods methotrexate is being used in an intermittent regimen with increasing frequency. Bone marrow toxicity, oral ulceration, and diarrhoea are all well-known side effects of this drug, but more recently renal toxicity (Condit et al., 1969) and chronic liver damage (Dahl et al., 1971) have been reported during or after methotrexate therapy. Pulmonary complications in patients with acute lymphoblastic leukaemia in remission treated with intermittent methotrexate therapy have been reported by the Acute Leukaemia Group B (1969), Clarysse et al. (1969), and Robertson (1970). We report a case of an acute, fatal respiratory illness with the pathological features of granulomata in the lungs. This occurred in a girl with acute lymphoblastic leukaemia in remission during maintenance therapy with intermittent methotrexate.

Case Report

A 6-year-old girl was admitted to hospital on 3 April 1970 with a history of general malaise and spontaneous bruising for one week. Examination showed an ill girl with a fever of 38°C, enlarged cervical and inguinal lymph nodes, a spleen palpable 3 cm below the left costal margin, and generalized bruising and petechiae. Haemoglobin 10·8 g/100 ml, M.C.H.C. 34%, platelets 56,000/mm³ total leucocyte count 45,000/mm³ (76% blasts, 2% metamyelocytes, 17% lymphocytes, 5% neutrophils). The bone marrow was hyper-